Genetic Health and Prenatal Diagnostics in Clinical Center Brcko District

Milenko Kolarski1, Aleksandar Krsić2, Stavko Nikić3, Gordana Joksic4, Goran Umicevic2, Zlatan Fatusic5, Jadranka Jovanovic Privrodić2, Zoran Petricic2

Institut za zdravstvenu zaštitu dece i omladine Vojvodine u Novom Sadu, Zavod za medicinsku genetiku, Novi Sad, Vojvodina, Srbija1

Akademia medicinskih nauka SLD, Beograd, Srbija2

Bolnica Brčko Distrikt, Ojdelenje ginekologije, Brčko, Bosna i Hercegovina3

Zavod za laboratorijsku dijagnostiku Aqualab, Beograd, Srbija4

Klinika za ginekologiju i akušerstvo, Univerzitetski klinički centar Tuzla, BiH5

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SUMMARY

We report genetic counseling and prenatal diagnostics in the Obstetrics and Gynecology Department of the Clinical Center Brčko District (BiH) which works for more than 4 years in prevention of giving birth to children with hereditary diseases and congenital malformations. Pregnant women from Brčko District, Tuzla Canton and wider area of BIH underwent genetic counseling. In the period from 2003 to 2007, 1234 pregnant women underwent amniocentesis and genetic counseling. Among them 27 foetuses with chromosome disorders were discovered (2.19%). There were 9 (0.72%) cases of autosomal numerical aberrations, 9 (0.72%) of numerical anomalies of sex chromosomes and 12 (1.07%) of structural chromosome aberrations. Chordocentesis was performed in 86 pregnant women: 7 foetuses were found carrying chromosome aberrations (8.14%). Frequency of chromosomes in comparison to the Centre of Medicine Genetics in the Children Clinic in Novi Sad (Serbia) indicates that it is significantly higher (1.67% compared to 2.19%), and in both cases the populations are significantly large (12210:1234) - there is a large difference in structural chromosomal aberrations (0.39% - 1.07%). This could point to harmful factors of the environment which contribute to induced genome damages.

Key words: genetic consulting, prenatal diagnostic, screening Down syndrome, Brčko District BiH.

1. INTRODUCTION

Genetic counseling and prenatal diagnostic of congenital anomalies is a one of most impotent improvements in prevent medicine in last century in the word (1,2,3). By starting with genetic counseling and prenatal diagnostics in the Clinical Center Brčko District, Bosnia and Hercegovina, Department for obstetrics and gynecology department, it has been started with diagnostics and prevention of giving birth to children with hereditary diseases and congenital malformations for the first time in country Bosnia and Hercegovina. Indications for prenatal diagnostics were: age of pregnant women above 35 and below 20, the most important and most often, as well as age of partners above 40; hereditary disease in a family; embryo or child with malformations; mental retardation in a family; repetitive spontaneous abortion; exposure to teratogens, consanguinity, and high risk Down syndrome after used ultrasound screening examination between 11-14GW (4) and 14-22GW (2).

The programs and strategies aimed to get genetically healthy offspring rely on activities of genetic counseling, non-invasive genetic ultrasound screening procedures, early screening SLD,11-14GW, late screening SLD,14-22GW. Testing of early genetic biochemical markers 11-14GW,(PAPP-A,Fbeta-hCG,estriol), with ultrasound screening marker Nuchal translucence and the late biochemical screening tripe test, (AFP,HCG,Estriol) with ultrasound screening marker,second trimester pregnant with Nuchal Fold Thickness and risc Down syndrome. Invasive prenatal diagnostic and genetic counseling and screening procedure (chorion villus aspiration biopsy at the 9-12GW,ultra-early amniocentesis in the 12-15GW,early amniocentesis between 15-20GW, cordocentesis between 20-24 GW). Cytogenetic examination were performed of cell obtained by all before mentioned invasive techniques, as well as targeted pre-and postnatal molecular genetic test on the monogenic diseases (5,6).

2. MATERIALS AND WORKING METHODS

During the period of 4 years, pregnant women, more exactly married couples from Brčko District, Tuzla's canton and wider area of BIH who came to Genetic counseling office of the Gynecology department of Clinical Center Brčko District, were treated carefully taking into account indications and ethical principles. A detailed anamnesis (76 questions), hereditary, detailed ultrasound Down syndrome screening during first trimester was performed, as well as ultrasound genetic markers of the first trimester. In all pregnancies where nuchal translucency showed higher values than is recommended (Nicolaide) amniocentesis was performed and obtained cells were analyzed cytogenetically. After 19 GW, cordocentesis was performed taking fetal blood out (19-21GW) when ultrasound, Down syndrome screening during second trimester pregnancy, showed nuchal thickness fold, up 6 mm (2). Improved ultrasound screening in the second trimester end MLR at her mathematical way discover Down syndrome in pregnancy (3).

All samples of amniotic fluid obtained in the 14-20 GW under ultrasound control have been sent to a cytogenetic laboratory for karyotyping. Furthermore, we perform ultrasound or other obstetrical monitoring where we include color dopler 4D (screening and diagnostics of congenital anomalies) and fetal echocardiographic diagnoses after 22GW, the last one is performed in other centers in Belgrade (6) in order to keep a pregnancy normal. Where it was necessary karyotype of both parents and members of the family has been analyzed. In cases where fetal anomalies were found and aberrant karyotype was found, report has been sent to ethical justification. Considering request of a pregnant woman and corresponding medical report, the ethical committee in its session gives permission for targeted abortion or fetus elimination.

3. RESULTS

In the period from 29/11/2003 to 22/12/2007, 1234 pregnant women were advised and amniocentesis was advised - data presented in Table 1. Population indicators from Brčko district are listed on Table 2.

In 27 fetuses, out of 1234, chromosome disorders were diagnosed, which gives 2.19%. (Figure 1). There were 9 cases (0.72%) with autosomal numerical aberrations, 9 (0.72%) cases carrying numerical anomalies of sex chromosomes and 12 (1.07%) carrying structural chromosome anomalies. Prenatally was diagnosed one case of Pallister- Killian Syndrome (mosaic 46, XX/47, XX+i12p),
first CTG-banding technique (Figure 3), and FISH with arm specific probe 12p technique (Figure 4).

Unique in the Western Balkan Region, specific in comparison to similar cases in literature; it was found in a pregnant woman aged 25 (these cases are described in literature for pregnant women above 38) with significant growth retardation (3 GW), what is also rare. Wenger et al (11) reported that advanced maternal age increases the risk of having a child with Pallister-Killian syndrome. Usually, i(12p) is maternal in origin (12). Maternal age at a conception is considered to be a significant risk factor in arising of trisomy and tetrasomy 12p as for the trisomy 21 (12). Tetrasomy 12p syndrome was independently cytogenetically (9) and clinically (8) postulated and diagnosed in the literature, and currently targeted FISH is the method of choice for detection of i (12p) in Pallister-Killian patients (10,12) as is shown in the Figure 4.

Cordocentesis was performed in 86 pregnant women. In 7 cases (8.14%) chromosome aberrations were found: Sy. Edwards 3 cases; Sy. Down 1 case; Sy. Klinefelter 1 case, Triplo X 1 case and mosaic 46XX/47,XXY/40 1 case. All 30 pregnancies with chromosomopathies (Figure 5) were terminated. It was determined that the pregnant women had 1,4 sexual intercourses per week before they got pregnant. The number of preg-

<table>
<thead>
<tr>
<th>2003</th>
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<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMNION</td>
<td>13</td>
<td>348</td>
<td>319</td>
<td>262</td>
<td>292</td>
</tr>
<tr>
<td>FET.BLOOD</td>
<td>3</td>
<td>14</td>
<td>18</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>PERIPHERAL BLOOD</td>
<td>3</td>
<td>80</td>
<td>19</td>
<td>38</td>
<td>32</td>
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**Table 1.** Live births samples, prenatal male karyotypes 618, prenatal female karyotypes 616.

<table>
<thead>
<tr>
<th>2003</th>
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<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>TOTAL</th>
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</thead>
<tbody>
<tr>
<td>LIVE BIRTH</td>
<td>13.20</td>
<td>10.30</td>
<td>2.90</td>
<td>2.90</td>
<td></td>
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<tr>
<td>DIED</td>
<td>13.09</td>
<td>10.53</td>
<td>2.56</td>
<td>2.57</td>
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</tr>
<tr>
<td>GROWTH RATE</td>
<td>12.97</td>
<td>11.02</td>
<td>1.95</td>
<td>1.95</td>
<td></td>
</tr>
<tr>
<td>INFANT MORTALITY</td>
<td>12.08</td>
<td>9.83</td>
<td>2.25</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>12.90</td>
<td>10.82</td>
<td>2.08</td>
<td>0.00</td>
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</tbody>
</table>

**Table 2.** Population Indicators From Brcko District (number of live birth, died, growth rate and infant mortality in Brcko District between 2003 to 2008, POPULACION PER 100. *14 years old were the youngest and 46 years old were oldest pregnancy.

Frequency of chromosomal aberrations in Brčko District was significantly higher in comparison to data of Centre of Medicine Genetics in the Children Clinic in Novi Sad (2,19 in Brčko compared to 1.67% in Novi Sad), and in both cases there are large populations (12 210:1234). Especially, there is a large difference in the incidence of structural chromosomal anomalies (1.07% Brčko: 0.39% Novi Sad). This could point to harmful factors of environment which could contribute in inducing genome damages. The number of sexual intercourse is the average is low and not enough to provide even simple reproduction, and that tells us something about changed living conditions and that is partly a cause that leads to reduced regeneration of population.

**4. DISCUSSION:**

Frequency of chromosomopathies diagnosed by prenatal diagnostics is high, and all pregnancies were terminated on request of pregnant woman and approval of Ethical committee before 24GW. Prenatal diagnosis discovers Down syndrome, other aneuploidies and structural

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**Figure 1.** Chromosome disorders diagnosed in our investigation.

**Table 3.** Chromosomal anomalies from amniotic fluid and fetal blood (27 samples) from brcko district (period of time 29.11.2003 – 22.12.2007)
eral chromosomal aberrations the most important goal in. Prenatal invasive di-
agnostic is fetal karyotyping. In Brčko District incidence of structural chromo-
somal aberrations is higher than in other regions in Western Balkan. The causes for
this have to be looked for, but the increase of structural anomalies especially points
to environment factors. Modern ethical principles were applied in the treatment
of families with discovered fetus chromo-
somalopathies. Indication criteria for prenatal
diagnostics and taking peripheral blood
for karyotyping are good, and that expla-
ins high frequency of chromosomopathies. Low number of sexual intercourses,
as one of modern life factors influences
decrease of reproduction. COST- bene-
fit analyses is very important for Brcko
District and all Bosnia and Hercegovina.
Discover only one fetus with Down syn-
drome, give is important benefit for many,
social safer family. Multidisciplinary, in-
ternationally approved different specia-
lis (doctors pediatrics, genetics, gyneco-
logist, biologist, psychologist, and other is
also important for good result in project
prevention birth babies with Down syn-
drome, other chromosomopathies and ba-
bies with congenital anomaly.
Prevention born bebis with Down syn-
drome is the best way only country
in the word for healthy population.

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Corresponding author: Mileno Kolarski,
MD. Institute for medical genetics, Novi Sad, Vojvodina, Serbia.